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(54) Title: COMPOSITIONS AND METHODS FOR TREATMENT OF PROLIFERATIVE DISORDERS

(57) Abstract: The present invention relates to compositions and methods for preventing and treating AIDS, AIDS-malignancy, and other tumors. In particular, this invention comprises modulation of mitogenic and angiogenic growth factors with lysyl oxidase and its homologues. In other aspects of this invention, lysyl oxidase and its homologues provide angiogenic inhibition to the transactivating protein Tat of HIV-1.

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## CLAIMS

What is claimed is:

1. A therapeutic composition for prophylaxis and treatment of a condition associated with an abnormal cellular proliferation, said composition comprising:
  - an effective amount of a therapeutically active portion of an inhibitor in a pharmaceutically acceptable inert carrier substance;
  - wherein said inhibitor inactivates a growth factor;
  - wherein said inhibitor oxidizes said growth factor at lysine residues; and
  - wherein said amount of said inhibitor is effective in preventing and treating a condition associated with said abnormal cellular proliferation.
2. A therapeutic composition for prophylaxis and inhibition of a condition associated with angiogenesis comprising:
  - an effective amount of a therapeutically active portion of an inhibitor in a pharmaceutically acceptable inert carrier substance;
  - wherein said inhibitor inactivates an angiogenic factor;
  - wherein said inhibitor oxidizes said angiogenic factor at lysine residues; and
  - wherein said amount of said inhibitor is effective in inhibiting said angiogenesis.
3. A therapeutic composition for prophylaxis and inhibition of a condition associated with a microorganism infection comprising:

an effective amount of a therapeutically active portion of an inhibitor in a pharmaceutically acceptable inert carrier substance;

5 wherein said inhibitor inactivates a transactivator for replication of said microorganism;

wherein said inhibitor oxidizes said transactivator at lysine residues; and

wherein said amount of said inhibitor is effective in inhibiting microorganism replication.

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4. The therapeutic composition of any of claims 1, 2, or 3, wherein said inhibitor is lysyl oxidase.

15 5. The therapeutic composition of any of claims 1, 2, or 3, wherein said inhibitor is a homologue of lysyl oxidase.

20 6. The therapeutic composition of any of claims 1, 2, or 3, wherein said lysyl oxidase is purified from bovine or other mammalian connective tissue.

25 7. The therapeutic composition of any of claims 1, 2, or 3, wherein said inhibitor is co-administered with a compound selected from the group consisting of an antineoplastic agent, a cytokine, a hormone, and a copper ion.

8. The therapeutic composition of any of claims 1, 2, or 3, wherein said condition is cancer.

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9. The therapeutic composition of any of claims 1, 2, or 3, wherein said condition is associated with a disease selected from the group consisting of breast cancer,

colon cancer, renal cancer, prostate cancer, ovarian cancer, lung cancer, brain cancer, skin cancer, embryo carcinoma, teratocarcinoma, germ cell tumor, uterine cancer, osteosarcoma, fibrosarcoma, melanoma, AIDS-associated malignancies, angiogenic diseases, other tumors, and hyperplastic diseases with or without inflammation.

10. The therapeutic composition of any of claims 1, 2, or 3, wherein said abnormal cellular proliferation is a tumor, lesion, or wound.

11. The therapeutic composition of claim 1, wherein said abnormal cellular proliferation is a human cell proliferation.

12. The therapeutic composition of claim 3, wherein said condition associated with a microorganism infection is AIDS.

13. The therapeutic composition of claim 3, wherein said microorganism is HIV-1.

14. The therapeutic composition of claim 3, wherein said transactivator for the replication of said microorganism is HIV-1 Tat.

15. A kit comprising a therapeutic composition of any of claims 1, 2, or 3 and instructions for use thereof.

16. A method of treating a patient believed to be at risk of suffering from a disease associated with abnormal

cellular proliferation, said method comprising the steps of:

- providing said patient; and
  - administering to said patient an effective amount of
- 5 the therapeutic composition of any of claims 1 or 2.

17. A method of modulating cellular proliferation and angiogenesis, said method comprising the steps of:

- contacting mitogenic and angiogenic factor with an
- 10 inhibitor in an effective amount to modulate cell proliferation, whereby said inhibitor is a therapeutic composition of any of claims 1 or 2; and
- determining regulation of cell proliferation.

15 18. A method of treating a patient believed to be at risk of suffering from a condition associated with a microorganism infection, said method comprising the steps of:

- providing said patient; and
- 20 administering to said patient an effective amount of the therapeutic composition of claim 3.

19. The method of any of claims 16, 17, or 18, wherein said disease is selected from the group consisting of

25 breast cancer, colon cancer, renal cancer, prostate cancer, ovarian cancer, lung cancer, brain cancer, skin cancer, embryo carcinoma, teratocarcinoma, germ cell tumor, uterine cancer, osteocarcinoma, fibrosarcoma, melanoma, AIDS-associated malignancies, angiogenic

30 diseases, other tumors and hyperplastic diseases with or without inflammation.

20. The method of any of claims 16 or 18, said method comprising the additional step of determining treatment progress by tissue biopsy.

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41 51 61 71 81 86  
 Tat: NH2-KALGISYGRK KRRQRRRAHQ NSQTHQASLS KQPTSQPRGD PTGPKE-COOH  
 107 117 127 137 146  
 FGF2: NH2-RSRKYTSWYV ALKRTGQYKL GSKTGPQGKA ILFLPMSAKS-COOH  
 123 133 143 153 163 165  
 VEGF165: NH2-RRKHLFVQDP QTCKCCKNT DSRCKARQLE LNERTCRCDK PRR-COOH  
 116 126 136 146 156  
 VEGF189: NH2-KSVRGKGKGQ KRKRKKSRYK SWSVPCGPCS ERRKHLFVQD POTCKCCKN  
 166 176 186 189  
 TDSRCKARQL ELNERTCRCD KPRR-COOH

**FIG. 3**